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ACCESSION NUMBER: 2005:471961 HCAPLUS Full-text

DOCUMENT NUMBER: 143:1314

TITLE: Use of 3-aza-1-oxa-dibenzo[e,h]azulenes for the  
manufacture of pharmaceutical formulations for the  
treatment and prevention of central nervous system  
diseases and disorders

INVENTOR(S): Marcep, Mladen; Mesic, Milan;

Pesic, Dijana; Dzapo, Iva

PATENT ASSIGNEE(S): Pliva-Istrazivacki Institut D.O.O., Croatia

SOURCE: PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

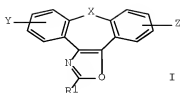
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005049036	A1	20050602	WO 2004-HR54	20041119
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2546591	A1	20050602	CA 2004-2546591	20041119
EP 1684766	A1	20060802	EP 2004-798733	20041119
EP 1684766	B1	20070627		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU				
CN 1901918	A	20070124	CN 2004-80039454	20041119
JP 2007512308	T	20070517	JP 2006-540631	20041119
AT 365556	T	20070715	AT 2004-798733	20041119
ES 2289573	T3	20080201	ES 2004-798733	20041119
IN 2006CN02229	A	20070608	IN 2006-CN2229	20060621
US 20070111990	A1	20070517	US 2006-595938	20060811
HK 1098670	A1	20080104	HK 2007-101111	20070131
PRIORITY APPLN. INFO.:			HR 2003-959	A 20031121
			WO 2004-HR54	W 20041119

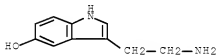
OTHER SOURCE(S): MARPAT 143:1314

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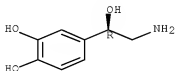
- AB The present invention relates to the use of compds. from the group of 3-aza-1-oxadibenzo[e,h]azulenes (I; X = heteroatom such as O, S, SO, SO<sub>2</sub>, (un)protected NH; Y, Z = H, halo, alkyl, alkenyl, hydroxy, amino, thiol, sulfonyl, cyano, nitro, etc.; R<sub>1</sub> = H, CHO, alkyl, carboxylic, etc.) and of their pharmacol. acceptable salts and solvates for the manufacture of a pharmaceutical formulation for the treatment and prevention of diseases, damages and disorders of the central nervous system (CNS) caused by disorders of the neurochem. equilibrium of biogenic amines or other neurotransmitters. Thus, an in vitro affinity of I compds. for binding to recombinant human 5-HT<sub>2A</sub> and 5-HT<sub>2C</sub> serotonin receptors expressed in CHO-K1 or COS-7 cells was determined using a radioligand. The radioligand binding was inhibited by the test compds. proportionally to the affinity of a certain compound for the receptor and to the concentration of the compound. Compds. showing IC<sub>50</sub> and K<sub>i</sub> in concns. lower than 1 μM were considered to be active. Compds. 1-oxa-8-thia-3-azadibenzo[e,h]azulene, dimethyl[2-(1-oxa-8-thia-3-azadibenzo[e,h]azulen-2-ylmethoxy)ethyl]amine, [2-(1-chloro-1-oxa-8-thia-3-azadibenzo[e,h]azulen-2-ylmethoxy)ethyl]dimethylamine, [2-(5-chloro-1-oxa-8-thia-3-azadibenzo[e,h]azulen-2-ylmethoxy)ethyl]dimethylamine and 5-chloro-2-methyl-1,8-dioxo-3-azadibenzo[e,h]azulene showed binding affinity to 5-HT<sub>2A</sub> and 5-HT<sub>2C</sub> receptors expressed as IC<sub>50</sub> value less than 200 nM and K<sub>i</sub> value less than 100 nM.
- IC ICM A61K031-55  
ICS A61K031-424; A61P025-00; A61P025-18; A61P025-22; A61P025-24
- CC 1-11 (Pharmacology)  
Section cross-reference(s): 63
- ST azaoxadibenzoazulene biogenic amine neurotransmitter nervous system disease; dibenzoazulene azaoxa biogenic amine neurotransmitter CNS disease
- IT Central nervous system, disease  
Human  
(azaoxa-dibenzoazulenes for treatment and prevention of CNS disorders by modulating biogenic amines or other neurotransmitters)
- IT Neurotransmitters  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(azaoxa-dibenzoazulenes for treatment and prevention of CNS disorders by modulating biogenic amines or other neurotransmitters)
- IT Amines, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(biogenic; azaoxa-dibenzoazulenes for treatment and prevention of CNS disorders by modulating biogenic amines or other neurotransmitters)
- IT 5-HT receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(type 5-HT<sub>2A</sub>, binding to; azaoxa-dibenzoazulenes for treatment and prevention of CNS disorders by modulating biogenic amines or other neurotransmitters)
- IT 5-HT receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(type 5-HT<sub>2C</sub>, binding to; azaoxa-dibenzoazulenes for treatment and prevention of CNS disorders by modulating biogenic amines or other neurotransmitters)

- IT Opioid receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (δ1-opioid, binding to; azaoxa-dibenzoazulenes for treatment and prevention of CNS disorders by modulating biogenic amines or other neurotransmitters)
- IT 50-67-9, Serotonin, biological studies 51-41-2,  
 Norepinephrine 51-61-6, Dopamine, biological studies  
 56-86-0, L-Glutamic acid, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (azaoxa-dibenzoazulenes for treatment and prevention of CNS disorders by modulating biogenic amines or other neurotransmitters)
- IT 612837-28-2, Dibenzo[2,3:6,7]thiopheno[4,5-d]oxazole  
 612837-29-3, Dibenzo[2,3:6,7]oxepino[4,5-d]oxazole  
 612837-30-6 612837-31-7 612837-32-3  
 612837-33-9 612837-34-0 612837-35-1  
 612837-36-2 612837-37-3 612837-38-4  
 612837-39-5 612837-40-8 612837-41-9  
 612837-42-0 612837-43-1 612837-44-2  
 612837-46-4 612837-47-5 612837-48-6  
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 612837-59-9 612837-60-2 612837-61-3  
 612837-62-4 612837-63-5 612837-64-6  
 612837-65-7 612837-66-8 612837-67-9  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (azaoxa-dibenzoazulenes for treatment and prevention of CNS disorders by modulating biogenic amines or other neurotransmitters)
- IT 50-67-9, Serotonin, biological studies 51-41-2,  
 Norepinephrine 51-61-6, Dopamine, biological studies  
 56-86-0, L-Glutamic acid, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (azaoxa-dibenzoazulenes for treatment and prevention of CNS disorders by modulating biogenic amines or other neurotransmitters)
- RN 50-67-9 HCAPLUS
- CN 1H-Indol-5-yl, 3-(2-aminoethyl)- (CA INDEX NAME)



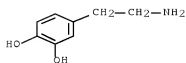
- RN 51-41-2 HCAPLUS
- CN 1,2-Benzenediol, 4-[(1R)-2-amino-1-hydroxyethyl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



- RN 51-61-6 HCAPLUS

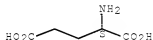
CN 1,2-Benzenediol, 4-(2-aminoethyl)- (CA INDEX NAME)



RN 56-86-0 HCAPLUS

CN L-Glutamic acid (CA INDEX NAME)

Absolute stereochemistry.



IT 612837-28-2, Dibenzo[2,3:6,7]thiepine[4,5-d]oxazole

612837-29-3, Dibenzo[2,3:6,7]oxepino[4,5-d]oxazole

612837-30-6 612837-31-7 612837-32-8

612837-33-9 612837-34-0 612837-35-1

612837-36-2 612837-37-3 612837-38-4

612837-39-5 612837-40-8 612837-41-9

612837-42-0 612837-43-1 612837-44-2

612837-46-4 612837-47-5 612837-48-6

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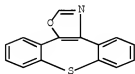
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612837-65-7 612837-66-8 612837-67-9

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(azaaza-dibenzoazulenes for treatment and prevention of CNS disorders  
by modulating biogenic amines or other neurotransmitters)

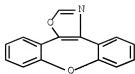
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CN Dibenzo[2,3:6,7]thiepine[4,5-d]oxazole (9CI) (CA INDEX NAME)



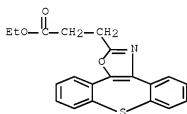
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CN Dibenzo[2,3:6,7]oxepino[4,5-d]oxazole (9CI) (CA INDEX NAME)



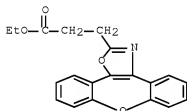
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CN Dibenzo[2,3:6,7]thiepine[4,5-d]oxazole-2-propanoic acid, ethyl ester (CA INDEX NAME)



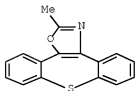
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CN Dibenz[2,3:6,7]oxepino[4,5-d]oxazole-2-propanoic acid, ethyl ester (CA INDEX NAME)



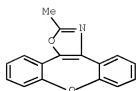
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CN Dibenzo[2,3:6,7]thiepine[4,5-d]oxazole, 2-methyl- (CA INDEX NAME)



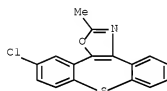
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CN Dibenz[2,3:6,7]oxepino[4,5-d]oxazole, 2-methyl- (CA INDEX NAME)



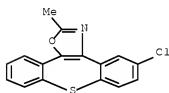
RN 612837-34-0 HCAPLUS

CN Dibenzo[2,3:6,7]thiepine[4,5-d]oxazole, 11-chloro-2-methyl- (CA INDEX NAME)



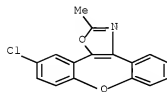
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CN Dibenzo[2,3:6,7]thiepine[4,5-d]oxazole, 5-chloro-2-methyl- (CA INDEX NAME)



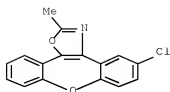
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CN Dibenz[2,3:6,7]oxepino[4,5-d]oxazole, 11-chloro-2-methyl- (CA INDEX NAME)



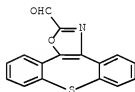
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CN Dibenz[2,3:6,7]oxepino[4,5-d]oxazole, 5-chloro-2-methyl- (CA INDEX NAME)



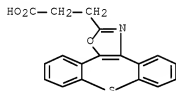
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CN Dibenzo[2,3:6,7]thiepine[4,5-d]oxazole-2-carboxaldehyde (CA INDEX NAME)



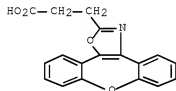
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CN Dibenzo[2,3:6,7]thiepine[4,5-d]oxazole-2-propanoic acid (CA INDEX NAME)



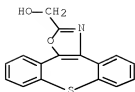
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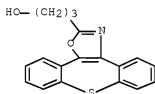
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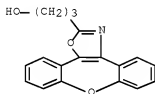
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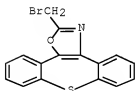
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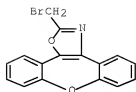
CN Dibenzo[2,3:6,7]thiepine[4,5-d]oxazole, 2-(bromomethyl)- (CA INDEX NAME)



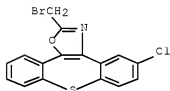
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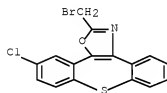




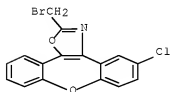
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 CN Dibenzo[2,3:6,7]thiepine[4,5-d]oxazole, 2-(bromomethyl)-5-chloro- (CA INDEX NAME)



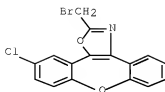
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 CN Dibenzo[2,3:6,7]thiepine[4,5-d]oxazole, 2-(bromomethyl)-11-chloro- (CA INDEX NAME)



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 CN Dibenzo[2,3:6,7]oxepino[4,5-d]oxazole, 2-(bromomethyl)-5-chloro- (CA INDEX NAME)

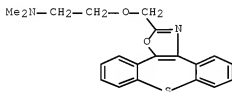


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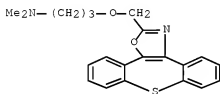
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CN Ethanamine, 2-(dibenzo[2,3:6,7]thiepine[4,5-d]oxazol-2-ylmethoxy)-N,N-dimethyl- (CA INDEX NAME)



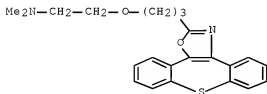
RN 612837-52-2 HCAPLUS

CN 1-Propanamine, 3-(dibenzo[2,3:6,7]thiepine[4,5-d]oxazol-2-ylmethoxy)-N,N-dimethyl- (CA INDEX NAME)



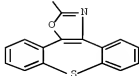
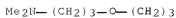
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CN Ethanamine, 2-(3-(dibenzo[2,3:6,7]thiepine[4,5-d]oxazol-2-ylpropoxy)-N,N-dimethyl- (CA INDEX NAME)



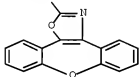
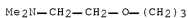
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CN 1-Propanamine, 3-(3-(dibenzo[2,3:6,7]thiepine[4,5-d]oxazol-2-ylpropoxy)-N,N-dimethyl- (CA INDEX NAME)



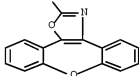
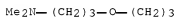
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CN Ethanamine, 2-(3-dibenz[2,3:6,7]oxepino[4,5-d]oxazol-2-ylpropoxy)-N,N-dimethyl- (CA INDEX NAME)



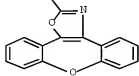
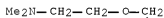
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CN 1-Propanamine, 3-(3-dibenz[2,3:6,7]oxepino[4,5-d]oxazol-2-ylpropoxy)-N,N-dimethyl- (CA INDEX NAME)



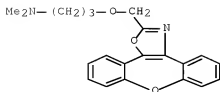
RN 612837-58-8 HCAPLUS

CN Ethanamine, 2-(dibenz[2,3:6,7]oxepino[4,5-d]oxazol-2-ylmethoxy)-N,N-dimethyl- (CA INDEX NAME)



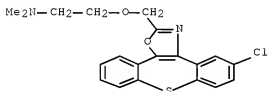
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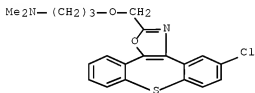
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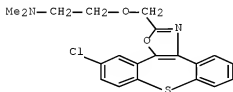
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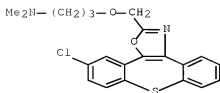
RN 612837-62-4 HCAPLUS

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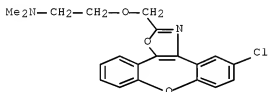
RN 612837-63-5 HCAPLUS

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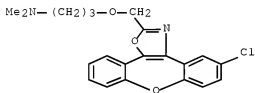
RN 612837-64-6 HCAPLUS

CN Ethanamine, 2-[(5-chlorodibenz[2,3:6,7]oxepino[4,5-d]oxazol-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)



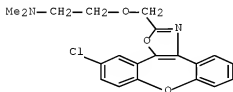
RN 612837-65-7 HCAPLUS

CN 1-Propanamine, 3-[(5-chlorodibenz[2,3:6,7]oxepino[4,5-d]oxazol-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)



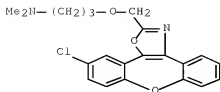
RN 612837-66-8 HCAPLUS

CN Ethanamine, 2-[(11-chlorodibenz[2,3:6,7]oxepino[4,5-d]oxazol-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)



RN 612837-67-9 HCAPLUS

CN 1-Propanamine, 3-[(11-chlorodibenz[2,3:6,7]oxepino[4,5-d]oxazol-2-yl)methoxy]-N,N-dimethyl- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:471937 HCAPLUS Full-text

DOCUMENT NUMBER: 143:1311

TITLE: Use of 1-oxadibenzo[e,h]azulenes for the manufacture of pharmaceutical formulations for the treatment and prevention of central nervous system diseases and disorders

INVENTOR(S): Mercep, Mladen; Mesic, Milan; Pesic, Dijana

PATENT ASSIGNEE(S): Pliva-Istrazivacki Institut D.O.O., Croatia

SOURCE: PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

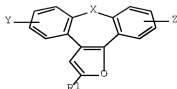
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TG, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
EP 1684742	A1	20060802	EP 2004-798731	20041119
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU			
JP 2007512306	T	20070517	JP 2006-540629	20041119
US 20070173493	A1	20070726	US 2006-595935	20060809
PRIORITY APPLN. INFO.:			HR 2003-955	A 20031121
			WO 2004-HR52	W 20041119

OTHER SOURCE(S): MARPAT 143:1311

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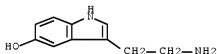


I

- AB The present invention relates to the use of compds. from the group of 1-oxadibenzo[e,h]azulenes (I; X = CH<sub>2</sub>, heteroatom such as O, S, SO, SO<sub>2</sub>, amino; Y, Z = H, halo, alkyl, haloalkyl, hydroxy, alkoxy, amino, thiol, sulfonyl, carboxy, cyano, nitro, etc.; R<sub>1</sub> = CHO, alkyl, amino, etc.) and of their pharmacol. acceptable salts and solvates for the manufacture of a pharmaceutical formulation for the treatment and prevention of diseases, damages and disorders of the central nervous system (CNS) caused by disorders of the neurochem. equilibrium of biogenic amines or other neurotransmitters, such as serotonin, norepinephrine and dopamine. Thus, an in vitro affinity of I compds. for binding to recombinant human 5-HT<sub>2A</sub> and 5-HT<sub>2C</sub> serotonin receptors expressed in CHO-K1 or COS-7 cells was determined using a radioligand. The radioligand binding was inhibited by the test compds. proportionally to the affinity of a certain compound for the receptor and to the concentration of the compound Compds. showing IC<sub>50</sub> and K<sub>i</sub> in concns. lower than 1 μM were considered to be active. Compound 2-[(11-chloro-1,8-dioxadibenzo[e,h]azulen-2-yl)-methoxy]ethyl]dimethylamine showed binding affinity to 5-HT<sub>2A</sub> and 5-HT<sub>2C</sub> receptors expressed as IC<sub>50</sub> value less than 200 nM and K<sub>i</sub> value less than 100 nM.
- IC ICM A61K031-343
- ICS A61K031-34; A61K031-38; A61K031-55; A61P025-00
- CC 1-11 (Pharmacology)
- Section cross-reference(s): 63
- ST oxadibenzoazulene biogenic amine neurotransmitter central nervous system disease; dibenzoazulene oxa biogenic amine neurotransmitter CNS disease
- IT Amines, biological studies
- RL: BSU (Biological study, unclassified); BIOL (Biological study) (biogenic; oxadibenzoazulenes for treatment and prevention of CNS disorders by modulating biogenic amines or other neurotransmitters)
- IT Central nervous system, disease
- Human (oxadibenzoazulenes for treatment and prevention of CNS disorders by modulating biogenic amines or other neurotransmitters)
- IT Neurotransmitters
- RL: BSU (Biological study, unclassified); BIOL (Biological study) (oxadibenzoazulenes for treatment and prevention of CNS disorders by modulating biogenic amines or other neurotransmitters)
- IT 5-HT receptors
- RL: BSU (Biological study, unclassified); BIOL (Biological study) (type 5-HT<sub>2A</sub>, binding to; oxadibenzoazulenes for treatment and prevention of CNS disorders by modulating biogenic amines or other neurotransmitters)
- IT 5-HT receptors
- RL: BSU (Biological study, unclassified); BIOL (Biological study) (type 5-HT<sub>2C</sub>, binding to; oxadibenzoazulenes for treatment and prevention of CNS disorders by modulating biogenic amines or other neurotransmitters)
- IT Opioid receptors
- RL: BSU (Biological study, unclassified); BIOL (Biological study) (δ1-opioid, binding to; oxadibenzoazulenes for treatment and

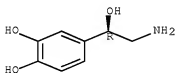
prevention of CNS disorders by modulating biogenic amines or other neurotransmitters)

- IT 50-67-9, Serotonin, biological studies 51-41-2,  
Norepinephrine 51-61-6, Dopamine, biological studies  
56-86-0, L-Glutamic acid, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(oxadibenzoazulenes for treatment and prevention of CNS disorders by  
modulating biogenic amines or other neurotransmitters)
- IT 199012-94-7D, Dibenzo[b,f]furo[2,3-d]oxepin, derivs.  
628262-96-4 628262-97-5 628262-98-6  
628262-99-7 628263-00-3 628263-01-4  
628263-02-5 628263-03-6 628263-04-7,  
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RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(oxadibenzoazulenes for treatment and prevention of CNS disorders by  
modulating biogenic amines or other neurotransmitters)
- IT 50-67-9, Serotonin, biological studies 51-41-2,  
Norepinephrine 51-61-6, Dopamine, biological studies  
56-86-0, L-Glutamic acid, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(oxadibenzoazulenes for treatment and prevention of CNS disorders by  
modulating biogenic amines or other neurotransmitters)
- RN 50-67-9 HCAPLUS
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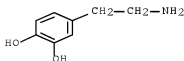


- RN 51-41-2 HCAPLUS
- CN 1,2-Benzenediol, 4-[(1R)-2-amino-1-hydroxyethyl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



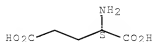
- RN 51-61-6 HCAPLUS
- CN 1,2-Benzenediol, 4-(2-aminoethyl)- (CA INDEX NAME)



- RN 56-86-0 HCAPLUS
- CN L-Glutamic acid (CA INDEX NAME)



Absolute stereochemistry.



IT 199012-94-7D, Dibenzo[b,f]furo[2,3-d]oxepin, derivs.

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628262-99-7 628263-00-3 628263-01-4

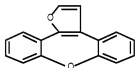
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Dibenzo[b,f]furo[2,3-d]oxepin-2-methanol 628263-05-8

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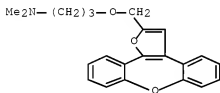
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CN Dibenzo[b,f]furo[2,3-d]oxepin (9CI) (CA INDEX NAME)



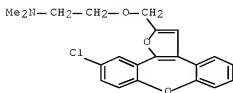
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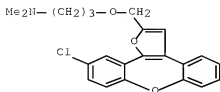
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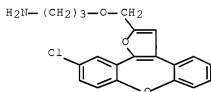
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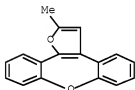
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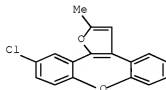
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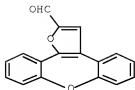
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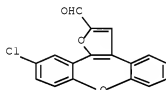
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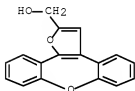
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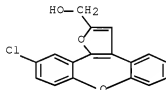
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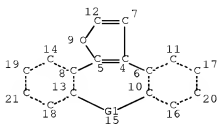
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DEFAULT ELEVEL IS LIMITED
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ACCESSION NUMBER: 2005:471937 HCAPLUS Full-text
DOCUMENT NUMBER: 143:1311
TITLE: Use of 1-oxadibenzo[e,h]azulenes for the manufacture
of pharmaceutical formulations for the treatment and
prevention of central nervous
system diseases and disorders
INVENTOR(S): Mercep, Mladen; Mesic, Milan; Pesic, Dijana
PATENT ASSIGNEE(S): Pliva-Istrazivacki Institut D.O.O., Croatia
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
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EP 1684742 A1 20060802 EP 2004-798731 20041119 <--

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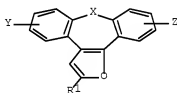
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PRIORITY APPLN. INFO.: HR 2003-955 A 20031121 <--

WO 2004-HR52 W 20041119

OTHER SOURCE(S): MARPAT 143:1311

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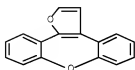
I

- AB The present invention relates to the use of compds. from the group of 1-oxadibenzo[e,h]azulenes (I; X = CH<sub>2</sub>, heteroatom such as O, S, SO, SO<sub>2</sub>, amino; Y, Z = H, halo, alkyl, haloalkyl, hydroxy, alkoxy, amino, thiol, sulfonyl, carboxy, cyano, nitro, etc.; R<sub>1</sub> = CHO, alkyl, amino, etc.) and of their pharmacol. acceptable salts and solvates for the manufacture of a pharmaceutical formulation for the treatment and prevention of diseases, damages and disorders of the central nervous system (CNS) caused by disorders of the neurochem. equilibrium of biogenic amines or other neurotransmitters, such as serotonin, norepinephrine and dopamine. Thus, an in vitro affinity of I compds. for binding to recombinant human 5-HT<sub>2A</sub> and 5-HT<sub>2C</sub> serotonin receptors expressed in CHO-K1 or COS-7 cells was determined using a radioligand. The radioligand binding was inhibited by the test compds. proportionally to the affinity of a certain compound for the receptor and to the concentration of the compound Compds. showing IC<sub>50</sub> and K<sub>i</sub> in concns. lower than 1 μM were considered to be active. Compound 2-[(11-chloro-1,8-dioxadibenzo[e,h]azulen-2-yl- methoxy)ethyl]dimethylamine showed binding affinity to 5-HT<sub>2A</sub> and 5-HT<sub>2C</sub> receptors expressed as IC<sub>50</sub> value less than 200 nM and K<sub>i</sub> value less than 100 nM.
- IT 199012-94-7D, Dibenzo[b,f]furo[2,3-d]oxepin, derivs.  
 628262-96-4 628262-97-5 628262-98-6  
 628262-99-7 628263-00-3 628263-01-4  
 628263-02-5 628263-03-6 628263-04-7,  
 Dibenzo[b,f]furo[2,3-d]oxepin-2-methanol 628263-05-8  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (oxadibenzoazulenes for treatment and prevention of CNS  
 disorders by modulating biogenic amines or other

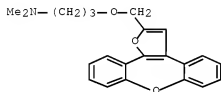
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RN 199012-94-7 HCAPLUS

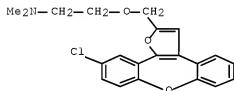
CN Dibenzo[b,f]furo[2,3-d]oxepin (9CI) (CA INDEX NAME)



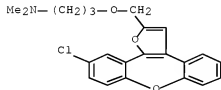
RN 628262-96-4 HCAPLUS

CN 1-Propanamine, 3-(dibenzo[b,f]furo[2,3-d]oxepin-2-ylmethoxy)-N,N-dimethyl-  
(CA INDEX NAME)

RN 628262-97-5 HCAPLUS

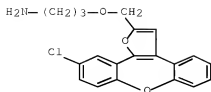
CN Ethanamine, 2-[(11-chlorodibenzo[b,f]furo[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl-  
(CA INDEX NAME)

RN 628262-98-6 HCAPLUS

CN 1-Propanamine, 3-[(11-chlorodibenzo[b,f]furo[2,3-d]oxepin-2-yl)methoxy]-  
N,N-dimethyl- (CA INDEX NAME)

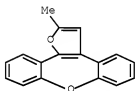
RN 628262-99-7 HCAPLUS

CN 1-Propanamine, 3-[(11-chlorodibenzo[b,f]furo[2,3-d]oxepin-2-yl)methoxy]-  
(CA INDEX NAME)



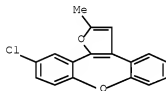
RN 628263-00-3 HCAPLUS

CN Dibenzo[b,f]furo[3,2-d]oxepin, 2-methyl- (CA INDEX NAME)



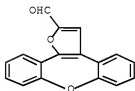
RN 628263-01-4 HCAPLUS

CN Dibenzo[b,f]furo[2,3-d]oxepin, 11-chloro-2-methyl- (CA INDEX NAME)



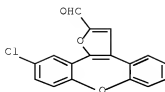
RN 628263-02-5 HCAPLUS

CN Dibenzo[b,f]furo[3,2-d]oxepin-2-carboxaldehyde (CA INDEX NAME)

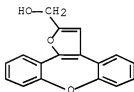


RN 628263-03-6 HCAPLUS

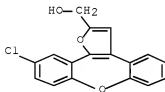
CN Dibenzo[b,f]furo[3,2-d]oxepin-2-carboxaldehyde, 11-chloro- (CA INDEX NAME)



RN 628263-04-7 HCAPLUS  
 CN Dibenzo[b,f]furo[3,2-d]oxepin-2-methanol (CA INDEX NAME)



RN 628263-05-8 HCAPLUS  
 CN Dibenzo[b,f]furo[3,2-d]oxepin-2-methanol, 11-chloro- (CA INDEX NAME)



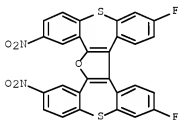
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 1983:143257 HCAPLUS [Full-text](#)  
 DOCUMENT NUMBER: 98:143257  
 ORIGINAL REFERENCE NO.: 98:21821a,21824a  
 TITLE: Neurotropic and psychotropic agents. CLXXIII.  
 Fluorinated tricyclic neuroleptics with prolonged  
 action: 3-fluoro-10-[4-(2-hydroxyethyl)piperazino]-  
 10,11-dihydrodibenzo[b,f]thiepins with less common  
 substituents in position 8  
 AUTHOR(S): Sindelar, Karel; Metysova, Jirina; Holubek, Jiri;  
 Svatek, Emil; Ryska, Miroslav; Protiva, Miroslav  
 CORPORATE SOURCE: Res. Inst. Pharm. Biochem., Prague, 130 60, Czech.  
 SOURCE: Collection of Czechoslovak Chemical Communications ( 1983), 48(1), 144-55  
 CODEN: CCCCAK; ISSN: 0366-547X  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 98:143257  
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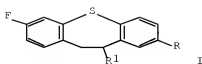




- AB Cyclization of 4,2-F(4-O2NC6H4S)C6H3CO2H gave 3-fluoro-8-nitrodibenzo[b,f]thiepin-10(11H)-one (I). I was reduced to II (R = NO2, R1 = OH) which was chlorinated to II (R = NO2, R1 = Cl) (III). Condensation of III with R2H gave II (R = NO2, R1 = R2). Also prepared were II (R = NH2, Ac, SO2NMe; R1 = R2). These II are central nervous system depressants and apomorphine antagonists. I (R = NO2, R1 = R2) had ED50 of 0.27 mg/kg orally in mice in the rotarod test after 2 h compared to 2.2 mg/kg for octoclotheptin.
- IT 85195-81-9P  
RL: SPN (Synthetic preparation); PREP (Preparation of preparation of)
- RN 85195-81-9 HCAPLUS
- CN Bisdibenzo[2,3,6,7]thiepin[4,5-b:4',5'-d]furan, 12,17-difluoro-3,7-dinitro- (9CI) (CA INDEX NAME)



- L15 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2008 ACS on STN
- ACCESSION NUMBER: 1982:85513 HCAPLUS [Full-text](#)
- DOCUMENT NUMBER: 96:85513
- ORIGINAL REFERENCE NO.: 96:14043a
- TITLE: Neurotropic and psychotropic agents. CLIV.  
Fluorinated tricyclic neuroleptics with prolonged action: 3-fluoro-8-halo derivatives of 10-piperazino-10,11-dihydrodibenzo[b,f]thiepins
- AUTHOR(S): Protiva, Miroslav; Sindelar, Karel; Metysova, Jirina; Holubek, Jiri; Ryska, Miroslav; Svatek, Emil; Sedivy, Zdenek; Pomykacek, Josef
- CORPORATE SOURCE: Res. Inst. Pharm. Biochem., Prague, 130 60, Czech.
- SOURCE: Collection of Czechoslovak Chemical Communications (1981), 46(8), 1788-99  
CODEN: CCCCAK; ISSN: 0366-547X
- DOCUMENT TYPE: Journal
- LANGUAGE: English
- OTHER SOURCE(S): CASREACT 96:85513
- GI



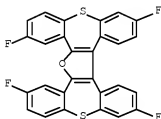
AB The title compds. I [R = F, R1 = 4-methylpiperazino; R = Br, iodo, R1 = 4-(2-hydroxyethyl)piperazino] were prepared by aminating I (R1 = Cl), obtained by chlorinating I (R1 = OH). The alcs. were obtained by reducing the ketones, prepared by cyclizing 5,2-F(HO2CCH2)C6H3SC6H4R-4 with polyphosphoric acid. I (R1 = substituted piperazino) have central nervous system depressant activity. Their structure-activity relationships are discussed.

IT 80709-39-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 80709-39-3 HCAPLUS

CN Bisdibenzo[2,3:6,7]thiépino[4,5-b:4',5'-d]furan, 3,7,12,17-tetrafluoro-  
(9CI) (CA INDEX NAME)



L15 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1980:146715 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 92:146715

ORIGINAL REFERENCE NO.: 92:23848h,23849a

TITLE: Neurotropic and psychotropic agents. CXXVII.  
Potential metabolites of tricyclic neuroleptics and  
their fluorinated analogs; 3-hydroxy-, 3-methoxy- and  
3-fluoro-10-(4-methylpiperazino)-10,11-  
dihydrodibenzo[b,f]thiépino

AUTHOR(S): Protiva, Miroslav; Sindelar, Karel; Sedivy, Zdenek;  
Metysova, Jirina

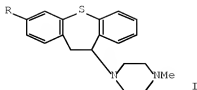
CORPORATE SOURCE: Res. Inst. Pharm. Biochem., Prague, 130 00/3, Czech.  
SOURCE: Collection of Czechoslovak Chemical Communications (1979), 44(7), 2108-23

CODEN: CCCCAK; ISSN: 0366-547X

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



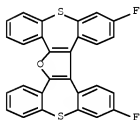
AB 4-Methoxy-2-(phenylthio)benzoic acid was transformed in 4 steps to the homologous acetic acid which was cyclized to 3-methoxydibenzo[b,f]-thiepin-10(11H)-one. Three further steps led to the 3-methoxy derivative of perathiepin (I, R = OMe) which was demethylated with BBr<sub>3</sub> to give I (R = OH). I (R = F) was prepared from (4-fluoro-2-iodophenyl)acetic acid, which was prepared by several procedures. Whereas I (R = OMe) had only mild tranquilizing activity, I (R = OH) was more potent than perathiepin in the tests for central depressant and cataleptic effects. I (R = F), while lacking the properties of a neuroleptic agent, was highly central depressant and this effect was prolonged after oral administration.

IT 73129-02-9F

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 73129-02-9 HCAPLUS

CN Bisdibenzo[2,3:6,7]thiepin[4,5-b:4',5'-d]furan, 12,17-difluoro- (9CI)  
(CA INDEX NAME)



L15 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1980:128852 HCAPLUS [Full-text](#)

DOCUMENT NUMBER: 92:128852

ORIGINAL REFERENCE NO.: 92:21015a,21018a

TITLE: Neurotropic and psychotropic agents. CXXIX.  
Fluorinated neuroleptics of the 10-piperazino-10,11-dihydrodibenzo[b,f]thiepin series; 6-fluoro derivatives of perathiepin, octoclothebin, doclothebin and some related compounds

AUTHOR(S): Cervena, Irena; Metysova, Jirina; Bartl, Vaclav;  
Protiva, Miroslav

CORPORATE SOURCE: Res. Inst. Pharm. Biochem., Prague, 130 00/3, Czech.  
SOURCE: Collection of Czechoslovak Chemical Communications (1979), 44(7), 2139-55

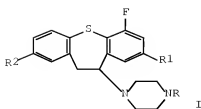
CODEN: CCCCAK; ISSN: 0366-547X

DOCUMENT TYPE: Journal

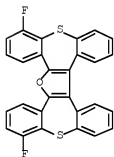
LANGUAGE: English

OTHER SOURCE(S): CASREACT 92:128852

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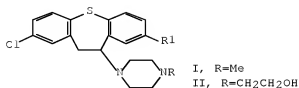


- AB 6-Fluoro-10-piperazino-10,11-dihydrodibenzo[b,f]thiepins I (R = Me, CH<sub>2</sub>CH<sub>2</sub>OH, R<sub>1</sub> = H, R<sub>2</sub> = H, Cl; R = Me, R<sub>1</sub> = Cl, R<sub>2</sub> = H) were prepared via 2-(2-fluorophenylthio)phenylacetic acids, 6-fluorodibenzo[b,f]thiepin-10(11H)-ones, the corresponding 10-hydroxy and 10-chloro compds. as intermediates. Fluorination in position 6 did not greatly influence the pharmacol. profile of the compds., indicating that hydroxylation in position 6 is only a minor metabolic pathway. I (R = Me, R<sub>1</sub> = Cl, R<sub>2</sub> = H) is a potent central depressant and neuroleptic agent with some protraction of the sedative effects. Many of the compds. also had bactericidal, fungicidal, and tuberculostatic activity.
- IT 73129-48-3F  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)  
 RN 73129-48-3 HCAPLUS  
 CN Bisdibenzo[2,3:6,7]thiophino[4,5-b:4',5'-d]furan, 1,9-difluoro- (9CI) (CA INDEX NAME)



- L15 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 1977:439416 HCAPLUS [Full-text](#)  
 DOCUMENT NUMBER: 87:39416  
 ORIGINAL REFERENCE NO.: 87:6219a,6222a  
 TITLE: Neurotropic and psychotropic agents. CV. Potential metabolites of noncataleptic neuroleptics: 2-chloro-8-hydroxy-10-(4-methylpiperazino)- and -10-[4-(2-hydroxyethyl)piperazino]-10,11-dihydrodibenzo[b,f]thiepin  
 AUTHOR(S): Valenta, V.; Bartl, V.; Dlabac, A.; Metysova, J.; Protiva, M.  
 CORPORATE SOURCE: Res. Inst. Pharm. Biochem., Prague, Czech.  
 SOURCE: Collection of Czechoslovak Chemical Communications (1976), 41(12), 3607-27  
 CODEN: CCCCAK; ISSN: 0366-547X

DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



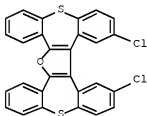
AB Starting from 5-chloro-2-(4-methoxyphenylthio)benzoic acid, 5 synthetic steps led to 2-chloro-8-methoxydibenzo(b,f)thiepin-10(11H)-one which was converted via 2 intermediates to 2-chloro-8-methoxy-10-(4-methylpiperazino)- and -10-[4-(2-hydroxyethyl)piperazino]-10,11-dihydrodibenzo(b,f)thiepin (I and II, R<sub>1</sub> = OMe). Demethylation with BBr<sub>3</sub> led to the title compds. I and II (R<sub>1</sub> = OH), which are potential metabolites of noncataleptic neuroleptics doclothepein and VUFB-10032 (I and II, R<sub>1</sub> = H). I and II (R<sub>1</sub> = OH and OMe) have central depressant and cataleptic effects, the methoxy derivs. being more active than the hydroxy derivs. (LD<sub>50</sub> and ED<sub>50</sub> given). Modified methods of preparing 5-chloro-2-(phenylthio)benzoic acid and the corresponding alc. were described.

IT 63186-55-0P 63186-56-1F

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

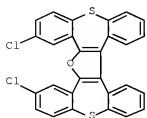
RN 63186-55-0 HCAPLUS

CN Bisdibenzo[2,3:6,7]thiepin[4,5-b:4',5'-d]furan, 13,16-dichloro- (9CI)  
 (CA INDEX NAME)



RN 63186-56-1 HCAPLUS

CN Bisdibenzo[2,3:6,7]thiepin[4,5-b:4',5'-d]furan, 3,7-dichloro- (9CI) (CA  
 INDEX NAME)



L15 ANSWER 7 OF 7 USPATFULL on STN

ACCESSION NUMBER: 2007:198145 USPATFULL Full-text  
 TITLE: 1-Oxadibenzo[e,h]azulenes for the treatment of  
 central nervous system  
 diseases and disorders  
 INVENTOR(S): Mercep, Mladen, Zagreb, CROATIA  
 Mesic, Milan, Zagreb, CROATIA  
 Pesic, Dijana, Sibenik, CROATIA  
 PATENT ASSIGNEE(S): Pliva-Istrazivacki Institut d.o.o., Zagreb, CROATIA,  
 10000 (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20070173493	A1	20070726
APPLICATION INFO.:	US 2004-595935	A1	20041119 (10)
	WO 2004-HR52		20041119
			20060809 PCT 371 date

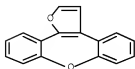
	NUMBER	DATE
PRIORITY INFORMATION:	HR 2003-20030955	20031121 <--
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	DARBY & DARBY P.C., P.O. BOX 770, Church Street Station, New York, NY, 10008-0770, US	
NUMBER OF CLAIMS:	15	
EXEMPLARY CLAIM:	1	
LINE COUNT:	941	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

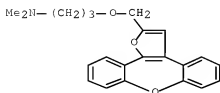
AB The present invention relates to the use of compounds from the group of 1-oxadibenzo[e,h]azulenes and of their pharmacologically acceptable salts and solvates in pharmaceutical formulation for the treatment and prevention of diseases, damages and disorders of the central nervous system (CNS) caused by disorders of the neurochemical equilibrium of biogenic amines or other neurotransmitters.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

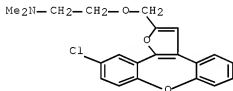
IT 199012-94-7D, Dibenzo[b,f]furo[2,3-d]oxepin, derivs.  
 628262-96-4 628262-97-5 628262-98-6  
 628262-99-7 628263-00-3 628263-01-4  
 628263-02-5 628263-03-6 628263-04-7,  
 Dibenzo[b,f]furo[2,3-d]oxepin-2-methanol 628263-05-8  
 (oxadibenzoazulenes for treatment and prevention of CNS disorders by  
 modulating biogenic amines or other neurotransmitters)  
 RN 199012-94-7 USPATFULL  
 CN Dibenzo[b,f]furo[2,3-d]oxepin (9CI) (CA INDEX NAME)



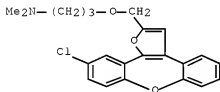
RN 628262-96-4 USPATFULL

CN 1-Propanamine, 3-(dibenzo[b,f]furo[2,3-d]oxepin-2-ylmethoxy)-N,N-dimethyl-  
(CA INDEX NAME)

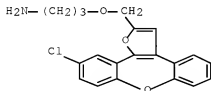
RN 628262-97-5 USPATFULL

CN Ethanamine, 2-[1(11-chlorodibenzo[b,f]furo[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl-  
(CA INDEX NAME)

RN 628262-98-6 USPATFULL

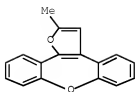
CN 1-Propanamine, 3-[1(11-chlorodibenzo[b,f]furo[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl-  
(CA INDEX NAME)

RN 628262-99-7 USPATFULL

CN 1-Propanamine, 3-[1(11-chlorodibenzo[b,f]furo[2,3-d]oxepin-2-yl)methoxy]-N,N-dimethyl-  
(CA INDEX NAME)

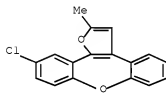
RN 628263-00-3 USPATFULL

CN Dibenzo[b,f]furo[3,2-d]oxepin, 2-methyl- (CA INDEX NAME)



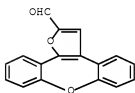
RN 628263-01-4 USPATFULL

CN Dibenzo[b,f]furo[2,3-d]oxepin, 11-chloro-2-methyl- (CA INDEX NAME)



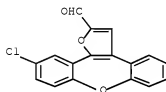
RN 628263-02-5 USPATFULL

CN Dibenzo[b,f]furo[3,2-d]oxepin-2-carboxaldehyde (CA INDEX NAME)



RN 628263-03-6 USPATFULL

CN Dibenzo[b,f]furo[3,2-d]oxepin-2-carboxaldehyde, 11-chloro- (CA INDEX NAME)

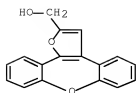


RN 628263-04-7 USPATFULL

CN Dibenzo[b,f]furo[3,2-d]oxepin-2-methanol (CA INDEX NAME)

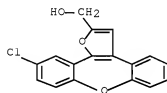


10/595,935



RN 628263-05-8 USPATFULL

CN Dibenzo[b,f]furo[3,2-d]oxepin-2-methanol, 11-chloro- (CA INDEX NAME)



## SEARCH HISTORY

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FILE 'HCAPLUS' ENTERED AT 13:14:35 ON 09 JUN 2008

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L2      72 SEA ABB=ON ("MESIC M"/AU OR "MESIC MILAN"/AU)
E PESIC DIJANA/AU
L3      71 SEA ABB=ON ("PESIC D S"/AU OR "PESIC DEJAN"/AU OR "PESIC
DIJANA"/AU)
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L5      2 SEA ABB=ON L4 AND 1(W)?OXADIBENZO?
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-1/BI OR 612837-44-2/BI OR 612837-46-4/BI OR 612837-47-5/BI OR
612837-48-6/BI OR 612837-49-7/BI OR 612837-50-0/BI OR 612837-51
-1/BI OR 612837-52-2/BI OR 612837-53-3/BI OR 612837-54-4/BI OR
612837-56-6/BI OR 612837-57-7/BI OR 612837-58-8/BI OR 612837-59
-9/BI OR 612837-60-2/BI OR 612837-61-3/BI OR 612837-62-4/BI OR
612837-63-5/BI OR 612837-64-6/BI OR 612837-65-7/BI OR 612837-66
-8/BI OR 612837-67-9/BI OR 628262-96-4/BI OR 628262-97-5/BI OR
628262-98-6/BI OR 628262-99-7/BI OR 628263-00-3/BI OR 628263-01
-4/BI OR 628263-02-5/BI OR 628263-03-6/BI OR 628263-04-7/BI OR
628263-05-8/BI)

```

FILE 'HCAPLUS' ENTERED AT 13:15:49 ON 09 JUN 2008

```

L7      2 SEA ABB=ON L5 AND L6

```

FILE 'REGISTRY' ENTERED AT 13:17:17 ON 09 JUN 2008

```

L8      STRUCTURE 628263-05-8
L9      1 SEA SSS SAM L8
L10     25 SEA SSS FUL L8

```

FILE 'HCAPLUS' ENTERED AT 13:19:13 ON 09 JUN 2008

```

L11     12 SEA ABB=ON L10
L12     6 SEA ABB=ON L11 AND (?CENTRAL?(W)?NERV?(W)?SYST? OR CNS OR
?NEUROCHEM?(W)?EQUIL? OR ?BIOGEN?(W)AMINE? OR ?NEUROTRANSMIT?)

```

FILE 'USPATFULL' ENTERED AT 13:21:10 ON 09 JUN 2008

```

L13     1 SEA ABB=ON L11 AND (?CENTRAL?(W)?NERV?(W)?SYST? OR CNS OR
?NEUROCHEM?(W)?EQUIL? OR ?BIOGEN?(W)AMINE? OR ?NEUROTRANSMIT?)

```

FILE 'HCAPLUS, USPATFULL' ENTERED AT 13:21:27 ON 09 JUN 2008

```

L14     7 DUP REMOV L12 L13 (0 DUPLICATES REMOVED)
L15     7 SEA ABB=ON L14 AND (PRD<20041119 OR PD<20041119)

```

FILE HOME

## FILE HCAPLUS

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## FILE REGISTRY

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STRUCTURE FILE UPDATES: 6 JUN 2008 HIGHEST RN 1026208-38-7

DICTIONARY FILE UPDATES: 6 JUN 2008 HIGHEST RN 1026208-38-7

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## FILE USPATFULL

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 5 Jun 2008 (20080605/PD)

FILE LAST UPDATED: 5 Jun 2008 (20080605/ED)

HIGHEST GRANTED PATENT NUMBER: US7383587

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